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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	**PAPER NUMBER**
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/460,605	Applicant(s) Disher
	Examiner Gollamudi Kishore, Ph.D	Art Unit 1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 21, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-8, 10, 13-20, 23, and 25-29* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-8, 10, 13-20, 23, and 25-29* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The request for the extension of time, filing under 1.114 and the preliminary amendment all dated 7-21-03 are acknowledged.

Applicant is reminded that any material added to the claims should be underlined and this has not been done in instant claim 1.

Claims included in the prosecution are 1-8, 10, 13-20, 23 and 25-29.

Claim Rejections - 35 U.S.C. § 112

1. **The following is a quotation of the first paragraph of 35 U.S.C. 112:**

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

2. **Claims 1-8, 10, 13-19, 23 and 25-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The expression 'non-peptide' now introduced in claim 1 in defining the super-amphiphilic molecules' has no support in the specification as originally filed and therefore, deemed to be new matter. A careful examination of the specification indicates that while there is support for the expression, wholly**

synthetic', there is no support in the specification for the negative limitation, 'non-peptide'.

3. **Claims 15-16, 18-19 and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for delivering the encapsulated active agents within the host system, does not reasonably provide enablement for removal of drugs, therapeutic composition, medicament genes, gene fragments and others recited in the claims (claim 29 for example). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.**

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described In re Wands, 8 USPQ2d, 1400 (Fed.Cir.1988). Among these factors are: (1) the nature of the invention; 2) the state of the prior art; 3) the relative skill of those In the art; 4) the predictability or unpredictability of the art; 5) the breadth of the claims; 6) the amount of direction or guidance presented; 7) the presence or absence of working examples; and 8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled In the art could not practice the invention without undue experimentation.

Instant invention is drawn to either delivery of active agents to an environment using polymersomes having within the said active agents or importing polymersomes to the

environment and removing agents from the environment. As noted from the specification, the agents removed include a variety of molecules such as waste products, , indicator, nutrient, vitamins, minerals, proteins, genes, biosealant and gas. The encapsulation of various active agents within liposomes and other forms such as micro spheres and nanospheres made from polymers for subsequent delivery, In the art of encapsulation is well-known and the relative skill of those In the art is reasonably high and the results are reasonably predictable. Methods of loading after the formation of the liposomes are also known In the art and the results are reasonable. However, it is unclear how one can administer the empty polymersomes and expect these polymersomes to pick up agents such as those listed above from the environment. The breadth of instant claims is very broad and instant specification does not provide adequate direction or guidance for a practitioner of the art. There are no working examples provided In the specification.

It would require undue experimentation to determine. It would require undue experimentation by one of ordinary skill In the art In determining whether the polymersomes would perform the claimed function. Broad claims must have broad basis of support In the specification; In the absence of such support, claims must be limited to polymersomes encapsulating active agents and the method of delivery of these agents to the host system.

4. **The following is a quotation of the second paragraph of 35 U.S.C. 112:**

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

5. **Claims 1-8, 10-19, 23, and 25-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

'the copolymer' on line 5 of claim 1 has no antecedent basis. Copolymer is recited In claim 2.

Claims 15-19, 23 and 27-29 provide for the use of the polymersomes, but, since the claim does not set forth any steps involved In the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 15-16, 21, 23, and 29 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved In the process, results In an improper definition of a process, i.e., results In a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Applicant's arguments have been fully considered, but are not found to be persuasive. The rejection is based on 'use claims'; The examiner suggests amending the

preamble: for example, " A method of transporting ------" In claim 15 instead of 'The method of using'.

It is unclear as to what material is removed from the environment as recited In claim 15 and patient In claim 16. These are method claims and therefore, should recite the step of 'how the polymersomes are removed' from the environment or from the patients. This is essential since according to claim 29 even components such as vitamins, nutrients, proteins, genes are removed from the patient. It is unclear as to how one can remove gene from a patient since genes are part of chromosomes. Furthermore, as pointed out before, claim 16 should recite as to how these materials are removed from the patient.

Claim 17 is a method of preparation of the polymersome claim dependent from a composition claim (claim 3). However, this claim does not recite preparation steps adequately.

Claim 18 is confusing. This claim's preamble recites 'a method of controlling the release of an encapsulated material'; yet the last line recites 'from the bulk surrounding the polymersome'. Since according to the last line, the active agent enters from the surroundings to the polymersome, this last line is inconsistent with the preamble, 'method of controlling the release. Since this is a method claim, the step of 'modulating the composition' should be defined In the claim (as to how it is modulated and where it is modulated).

The distinction between a 'drug', 'a therapeutic composition' and a 'medicament' In claims 14, 23 and 28 is unclear. Similar is the case with a 'nutrient', 'sugar', 'vitamin' and a 'mineral' (also In claim 14). In claim 14, it is unclear what 'waste product' is intended to convey. Applicant's arguments have been fully considered, but are not found to be persuasive since no evidence is provided. The only reference cited by applicant is Grant & Hackh's Dictionary for the definition of the term, 'drug'. As evidenced by the definition given In the dictionary itself, a drug is a 'medicinal substance' and instant claims recite 'medicament' besides 'drug'.

This rejection is maintained since applicant has not addressed this issue.

Furthermore, one of the materials delivered as recited In claims 23 and 29 is an encapsulated 'waste product'. It is unclear as to why one would deliver a waste product. It is also unclear as to where it is delivered. The examiner has already responded to applicant's arguments with regard to removal of components such as nutrients and other beneficial agents from the patient (see previous action).

The examiner suggests a careful review of the claims and restructuring them.

Claim Rejections - 35 U.S.C. § 102

6. **The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made In this Office action:**

A person shall be entitled t a patent unless --

(b) the invention was patented or described In a printed publication In this or a foreign country or In public use or on sale In this country, more than one year prior to the date of application for patent In the United States.

(a) the invention was known or used by others In this country, or patented or described In a printed publication In this or a foreign country, before the invention thereof by the applicant for a patent.

7. Claims 1-4, 6, 10, 13-16 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Ding (J. Phys. Chem., 1998) or Fendler (Science, 1984) all are of record.

The above references teach polymeric vesicles having a membrane; the polymers are diblock polymers (note abstracts In each). The references meet the requirements of instant claims.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant amends claim 1 to recite 'wherein the membrane is formed In an aqueous solution without the use of organic solvent', 'without the post assembly stabilization by cross-linking' and argue that these limitations distinguish instant claims from Ding's. This argument is not found to be persuasive since as pointed out before, instant claims are product by process claims and therefore, considered as product claims; applicant has not shown that Ding's vesicles after formation are patentably distinct from instant vesicles. With regard to applicant's arguments that neither of Ding's polymer blocks favor aqueous solution as a hydrophilic polymer does by definition, the examiner points out that Ding teaches hydroxylation of PI chains thereby making the product water

soluble In the paragraph bridging pages 6108 and 6109. The very fact that the product is water soluble indicates that the polymer has a hydrophilic part In the molecule.

Applicant's arguments with regard to Fendler are not found to be persuasive. Applicant argues that Fendler teaches vesicle assembly only from polymerizable lipids which are not super-amphiphilic molecules that are polymeric, having a number average molecular weight _> 1400. This argument is not found to be persuasive since according to instant claim 1, the membrane comprises one or more wholly synthetic super-amphiphilic molecules that are polymeric and according to Fendler, the surfactants are polymerized molecules and since they have both hydrophobic and hydrophilic segments they are amphiphilic In nature. In other words, instant claims do not distinguish over Fendler. The examiner suggests naming specific polymers if they wish to over the prior art's polymers.

Upon consideration, the 102 rejections over Cornelissen, Hentze, and Liu are withdrawn.

Claim Rejections - 35 U.S.C. § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth In this Office action:

> **(a) A patent may not be obtained though the invention is not identically disclosed r described as set forth In section 102 of this title, if the differences between the subject matter s ught t be patented and the prior art are such that the subject matter as a whole would have been obvi us at the time the invention was made to a person having rdinary skill In the art to which said subject matter pertains. Patentability shall not be negatived by the manner In which the invention was made.**

9. Claims 3-6, 10 and 14-20, 23 and 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ding or Fendler cited above.

The references of Ding, and Fendler are suggestive of the potential applications of the polymeric vesicles for the drug delivery. The use of the polymeric systems taught by Ding or Fendler for drug delivery would have been obvious to one of ordinary skill In the art since these references are suggestive of the drug delivery. As pointed out above, since some of the administered polymersomes are excreted by the host system, 'removal from the environment would have been obvious to one of ordinary skill In the art. The criticality of a triblock polymer is not readily apparent to the examiner since from the references it would appear that the amphiphilic nature of the polymer is the determinant factor.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant's arguments once again are based on presumed lack of teachings of vesicles In the prior art. These arguments have been addressed above. As to applicant's arguments that none of the references teaches the use of the vesicles for drug delivery, the examiner points out that all of the references cited clearly teach the application of these polymers for drug delivery.

10. Claims 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ding or Fendler cited above, further In view of Kirpotin (FEBS Letters, 388, (1996), PP. 115-118).

The teachings of Ding, and Fendler have been discussed above. What is lacking In Ding, or Fendler is the inclusion of other phospholipids In the vesicle compositions.

Kirpotin discloses liposomes made from a combination of polymers and phospholipids such as DOPE (note the abstract).

The inclusion of vesicle forming phospholipids In the vesicular compositions of Ding or Fendler with a reasonable expectation of success, would have been obvious to one of ordinary skill In the art since the reference of Kirpotin teaches that vesicles can be formed from a combination of polymers and small phospholipids and such vesicles are stable.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.

The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-3592.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

All Internet e-mail communications will be made of record In the application file. PTO employees do not engage In Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth In the Interim Internet Usage Policy published In the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-1235.

Gollamudi S. Kishore, Ph. D

Primary Examiner

Group 1600

gsk

October 17, 2003